Editorials

On 'Downsizing' Health Care

AS THIS IS WRITTEN, two giants of American economic growth and industrial achievement are undergoing unprecedented "downsizing," that is, they are substantially reducing the size of their organizations and the scope of their industrial operations. General Motors Corporation (GM) and International Business Machines, Inc (IBM) were considered among the best in the industrial world. They set standards for American enterprise and technologic success. Both prospered, but as they did, their corporate infrastructure grew and with it, the number of employees and the costs of administering and operating such large, complex organizations. The needs and interests of the corporate infrastructure began to displace the perceived needs and interests of the public that was to consume their products. General Motors began to build large cars when the public wanted small ones, and IBM placed its bets on large mainframe computers while the public was turning to smaller computers that could be linked to one another more or less as needed. Both began to lose money, and the costs, which were rising, finally became unacceptable. The corporate solution mandated by the rising and uncontrollable costs was to downsize what had been paragons of American economic growth and achievement. This was done by closing unprofitable plants, eliminating a great many jobs, and trying to be more responsive to consumer needs and expectations.

There would seem to be some parallels in health care. American health care is generally considered to be the best in the world. It is certainly the most technologically advanced. It has surely prospered. The infrastructure and the number of jobs within the health care system have grown enormously. The costs continue to rise and are now considered by many to be unacceptable. The system's interests are not always responsive to what the public or health care consumers need or expect. Nearly 30 million Americans have no health insurance with which to access the system. Yet America spends more dollars per capita on health care than any other developed nation. Other industrialized nations seem to be doing better. One can make an argument for a parallel need to downsize the American health care system and for some better responsiveness to consumer needs.

Corporations are at an advantage for accomplishing effective downsizing within their organizations. There is relatively centralized control. The corporate executives and the boards of directors represent the stockholders who in fact own the company. They are in a position to restructure the system from within by fiat. They can be ruthless and fire employees and close unprofitable plants more or less at will to accomplish the needed downsizing. And perhaps equally important, they need to serve only those consumers who are willing and able to pay for their products or services.

The health care system, on the other hand, is at a comparative disadvantage when it comes to downsizing. Power in the system is spread widely and is therefore diffuse. It is unlikely, if it has not already been demonstrated, that in this nation any single authority will ever be able to govern health care. The ownership is widely distributed throughout both the public and private sectors. It is now the largest industrial enterprise in the nation. There are many jobs, professions, and other entrenched political forces to be taken into account. And, further, the system must somehow serve those who cannot pay for needed products or services that the system provides. Yet, some form of downsizing seems as necessary for a high-cost health care system as it has proved to be for GM and IBM and for many of the same reasons.

There are similarities between what must be done in GM and IBM and what must be done in health care. Both need to pay more attention to consumer needs and expectations. Both need to improve efficiency and reduce the cost per consumer served. Both need to promote and accommodate progress and change. Both need to increase the size of their market and serve more consumers.

In health care there may already be more than enough dollars, since we are already spending more per capita than any other nation. There are many underserved consumers who receive inadequate or inefficient care—or none at all. Downsizing in health care might better be viewed as downsizing the enormous and ever-increasing overhead waste and inefficiency that now pervade the system and somehow reallocating the dollars thus saved to meet the basic needs of all consumers and, of course, including those who are presently without adequate access. Done well, this could stabilize the rise in health care costs, increase the size of the consumer market for health care, and avoid too great an overall job loss in the health care system. Downsizing in health care would then eliminate much of today's costly excess baggage, but this would be eased by a countervailing extension of products and services to a presently underserved market. However, the temptation to do this by fiat should be resisted because, unlike GM and IBM, the health care system is multifocal with a wide range of ownerships and power bases, and all must act in concert if there is to be efficiency and ultimate success. Collaboration rather than coercion would seem more likely to achieve a desired result. Even so, there may be lessons to be learned from the downsizing experiences of GM and IBM.

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Hansen's Disease—A Time for Cautious Optimism

HANSEN'S DISEASE, or leprosy, is an ancient human malady. The causative organism, *Mycobacterium leprae,* is an exquisitely adapted human pathogen, capable of multiplying to incredible numbers in susceptible hosts while

rarely killing its victims. Similarly, the innate resistance present in 80% to 90% of the population is consistent with long-term selective pressure on the genetics of the human immune system. Whereas complete control or eradication of leprosy is not a realistic goal for the foreseeable future (despite the wishful thinking of the World Health Organization[1]), the world situation with respect to leprosy is more hopeful than at any time in the past 20 years.

The historical epidemiology of leprosy in the United States and western Europe is complex and controversial, but there is universal agreement that the prevalence of leprosy rapidly declined in the late 1800s and that the disease had virtually disappeared from many countries (including Norway, the home of Armauer Hansen) by the 1920s. The explanation for this phenomenon, which took place decades before the discovery of effective chemotherapy, is unknown. This is in stark contrast to the situation in many developing countries of Africa, South America, Southeast Asia, and the Indian subcontinent. Leprosy continued virtually unchecked in these regions, despite control programs initially based on the principle of isolation and subsequently on single-drug therapy with dapsone. In 1966 it was estimated that there were approximately 11 million cases of leprosy in the world. Estimates over the next two decades were consistently in the range of 10 to 12 million cases. This may not be as dismal as it first appears, since the population at risk more than doubled over this 20-year period, but it was discouraging to leprosy workers who had hoped for more dramatic evidence of the efficacy of their control programs.

This evidence may now be in hand. Global epidemiologic data are notoriously suspect, particularly when the disease in question primarily affects the rural poor in developing countries. Nonetheless, there is a growing body of evidence suggesting that dramatic changes have recently taken place in the epidemiology of Hansen's disease. New data from the World Health Organization estimate that the number of active cases of leprosy in the world in 1991 had decreased to 5.5 million.[2] Noordeen and co-workers speculate that this dramatic change likely reflects many concurrent developments: the implementation of multidrug therapy in the early 1980s with its shorter treatment durations and precise definitions of cure, increased leprosy surveillance efforts as part of the multidrug-treatment program, possible residual effects from preexisting dapsone monotherapy programs, and naturally declining trends in some areas. Fine thinks that intensive vaccination programs with bacillus Calmette-Guérin (BCG) may have also contributed to this striking decrease.[1]

There is more good news in the area of chemotherapy for leprosy. The move to multidrug-treatment regimens in the early 1980s was primarily a response to the concern over the rapidly increasing problem with dapsone resistance. So-called secondary dapsone resistance developing in multibacillary patients after years of dapsone monotherapy and manifesting as recrudescence of active clinical disease had been recognized for many years. It was not until the late 1970s, however, that dapsone resistance in newly diagnosed patients (primary dapsone resistance) became a substantial problem. There was also growing concern about the possible emergence of rifampin and clofazimine resistance. It rapidly became apparent that the additional difficulty and expense of treating patients with resistant disease offset the disadvantages of multidrug therapy—increased drug costs, supervised administration, and toxicity. By the mid-1980s most countries had adopted some variant of multidrug therapy.

It is fair to say that the results have exceeded expectations. The prevalence of high-level dapsone resistance, particularly primary resistance, has not increased and may be on the decline. Resistance to other antimycobacterial agents remains extremely uncommon. Many patients who had been maintained on clinic rosters for years were declared cured and were discharged. This in turn freed up personnel and funds for associated activities such as case finding and rehabilitative care for patients with residual deformities (estimated to number 2 to 3 million worldwide).[2]

Stable or diminishing drug resistance and the apparent effectiveness of a shorter duration of chemotherapy is not the end of the good news. In contrast to the dismal situation with *Mycobacterium tuberculosis* and *Mycobacterium avium,* in recent years several new agents with excellent activity against *M leprae* have been developed and tested, including minocycline, ofloxacin, and clarithromycin. Several other agents including fusidic acid, brodimoprim, various clofazimine derivatives, and the combination of imipenem and cilastatin sodium have also shown some promise. Given their high cost relative to the currently used drugs, it is unclear exactly what role these new agents will play in the routine management of Hansen's disease. While there is some hope that enhanced bactericidal activity will make shorter treatment courses possible, the slow multiplication rate and low metabolic activity of *M leprae* may be limiting factors. Antibiotics, in common with essentially all chemotherapeutic agents, exhibit maximal activity against actively replicating and metabolically active cells. The lethargic nature of *M leprae* may place practical limits on the minimum duration of chemotherapeutic regimens. Still, for the foreseeable future, and certainly for the remainder of this decade, the world possesses an adequate therapeutic armamentarium to treat Hansen's disease.

In the past decade there have also been dramatic advances in our understanding of disease pathogenesis and host immunity in leprosy. The cellular constituents of leprosy lesions have been characterized for the different classes of disease, and the web of cytokine interactions is slowly being untangled.[3] A good example of the clinical importance of this work is seen in our new understanding of erythema nodosum leprosum, a common and sometimes life-threatening complication of multibacillary leprosy. Erythema nodosum leprosum was long thought to be an immune complex disease, based on clinical and histopathologic similarities to experimental and naturally occurring immune complex diseases. This hypothesis, however, failed to explain the therapeutic efficacy of

thalidomide, which has no activity in classical immune complex disorders, or the fact that immune complexes could not be consistently detected in patients with erythema nodosum leprosum. In 1987, we reported that cyclosporine, a specific inhibitor of interleukin-2 activity, was effective in controlling recalcitrant cases of erythema nodosum leprosum.[4] More recently it has been shown that levels of tumor necrosis factor-α (TNFα) are elevated in patients with this reaction and that thalidomide acts by selectively inhibiting TNFα.[5] If this finding is confirmed, there is a strong possibility that one or more of the anti-TNF agents currently under development will provide a therapeutic alternative for erythema nodosum leprosum without the toxicity of thalidomide or cyclosporine.

Despite these dramatic developments, there remain several areas of concern or where further research is needed. It is critical that existing control programs in endemic areas be sustained or enhanced. It is also essential that clinicians remain vigilant for the emergence of drug resistance and that research into new drug development continue. The recent experience with tuberculosis should be a lesson in the hazards of complacency and the necessity to maintain a strong control program even when a disease is waning in prevalence.

There is a need for epidemiologic studies to document the extent of the decrease in the prevalence of leprosy and to gather accurate information on the incidence of leprosy. These studies might also help to resolve the uncertainty concerning the mode of transmission of *M leprae*.[6] A rapid decline in disease incidence during an active multidrug therapy-based control program would be consistent with a primary role for human-to-human transmission, whereas a stable or slowly declining incidence might suggest acquisition of *M leprae* infection from the environment. Taken to its logical conclusion, if epidemiologic studies indicate that *M leprae* is simply one of the numerous species of environmental mycobacteria, then simple measures such as providing clean water or shoes for children might be the most cost-effective control strategy.

Progress towards the goal of eradication will also depend on continued support for basic research. There is a desperate need for a diagnostic test that can be done under field conditions by personnel without advanced laboratory or pathology training. As summarized by Gelber, existing serologic tests lack sufficient predictive value for active disease.[6] Preliminary results with assays using the polymerase chain reaction are more promising, but much remains to be done. Improved methods for antimicrobial sensitivity testing would greatly accelerate the process of screening novel compounds for activity against *M leprae* and for detecting drug resistance. Finally, there remains the hope that the growing understanding of the immunology of leprosy will facilitate the design of a vaccine that will consistently produce protective immunity.[7]

These are exciting and optimistic times in the field of leprosy. The work of innumerable researchers and health care professionals is finally beginning to bear fruit, and there is the real possibility of continued dramatic declines in the number of cases. At the same time, it must be remembered that the worldwide epidemic of human immunodeficiency virus infection is placing unprecedented demands on the limited health care budgets of many of the countries where leprosy is highly endemic. The next decade promises to be as exciting and eventful as the one that has just drawn to a close.

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REFERENCES

1. Fine PEM: Reflections on the elimination of leprosy. Int J Lepr Other Mycobact Dis 1992; 60:71-80
2. Noordeen SK, Bravo LL, Sundaresan TK: Estimated number of leprosy cases in the world. Bull WHO 1992; 70:7-10
3. Yamamura M, Uyemura K, Deans RJ, et al: Defining protective responses to pathogens: Cytokine profiles in leprosy lesions. Science 1991; 254:277-279
4. Miller RA, Shen JY, Rea TH, Harnisch JP: Treatment of chronic erythema nodosum leprosum with cyclosporine A produces clinical and immunohistologic remission. Int J Lepr Other Mycobact Dis 1987; 55:441-449
5. Sampaio EP, Sarno EN, Galilly R, Cohn ZA, Kaplan G: Thalidomide selectively inhibits tumor necrosis factor-α production by stimulated human monocytes. J Exp Med 1991; 173:699-703
6. Gelber R: Hansen's disease. West J Med 1993; 158:583-590
7. Bretscher PA: A strategy to improve the efficacy of vaccination against tuberculosis and leprosy. Immunol Today 1992; 13:342-345

The Enigma of Graves' Ophthalmopathy

AN EXPLANATION FOR THE ASSOCIATION of hyperthyroidism with eye disease has long been sought. In 1835, Robert Graves described the case of a 20-year-old woman with weakness on exertion, weight loss, and tachycardia[1(p36)]:

[T]he eyes assumed a singular appearance, for the eyeballs were apparently enlarged, so that when she slept or tried to shut her eyes, the lids were incapable of closing. When the eyes were open, the white scler[ae] could be seen to a breadth of several lines, all around the cornea. In a few months, the action of the heart continuing with unceasing violence, a tumor of a horseshoe-shape appeared in the front of the throat and exactly in the situation of the thyroid gland.

Although advances have been made in our understanding of Graves' ophthalmopathy since this early description, we still lack the insight needed to design all but essentially palliative therapy for our patients with this disorder.

Investigations concerning the pathogenesis of Graves' ophthalmopathy have been difficult to undertake, largely because there is no animal model for this condition and because of the relative scarcity of affected human orbital tissues available for study. Because the hyperthyroidism of Graves' disease is caused by circulating antibodies directed against a thyroid antigen (the thyroid-stimulating hormone [TSH] receptor), early studies of ophthalmopathy were aimed at detecting autoantibodies directed against orbital antigens. These studies were complicated by the use of porcine tissues by investigators lacking access to human tissues and by the use of crude human tissue preparations that did not allow an exact definition of the cells being studied. Indeed, even today there remains controversy concerning precisely which orbital cell is the target of autoimmune attack in the disease. In addition, it